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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,937	02/15/2002	Herbert M. Dean	dean0202con	3941

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EXAMINER

HUI, SAN MING R

ART UNIT PAPER NUMBER

1617

DATE MAILED: 09/30/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/076,937

Applicant(s)

DEAN ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 June 2003 and 14 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 11-16 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18 is/are allowed.
- 6) ☒ Claim(s) 1-10 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 26, 2003 has been entered.

Warning

Applicant is advised that should claim 1 be found allowable, claim 17 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims are drawn to composition comprising the same components.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearle (American Heart Journal, 1990 Sep; 120(3):739-742), Carruthers et al. (American Journal of Cardiology, 1993;71:575-581), Abby et al. (Journal of the American Board of Family Practice, 1998; 11(5):391-398), Oakley et al. (The Journal of Nutrition, 1996;126(3): 751S – 755S), and Behounek et al. (US Patent 5,691,375) in view of Rork et al. (US Patent 5,882,682), references of record.

Pearle teaches that beta-blockers such as timolol, metoprolol, atenolol, and propranolol reducing the overall mortality and the incidence of recurrent myocardial infarction (See the abstract; also page 740, col. 1, second paragraph).

Carruthers et al. teaches atenolol reducing the risk of coronary heart disease (See the abstract).

Abby et al. teaches folic acid and vitamin B₆ are useful in reducing the risk of coronary heart disease such nonfatal myocardial infarction and fatal coronary heart disease (See particularly page 395, Table 2).

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Oakley et al. teaches vitamin B₁₂ supplement is useful with folic acid administration to avoid the folic acid adverse effect: B₁₂ deficiency (See page 3, third and fourth paragraph).

Behounek et al. teaches HMG-CoA reductase inhibitor such as pravastatin is useful in reduce the risk of cardiovascular event (See the abstract).

The references do not expressly the incorporation of beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B₆, and vitamin B₁₂ into a single once-a-day dosage unit.

Rork et al. teaches a sustained release system that can include beta-blockers such as timolol, metoprolol, atenolol, and propranolol and statin cholesterol lowering agents such as simvastatin, pravastatin, and lovastatin (See col. 6, line 64-66 and col. 7, line 16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B₆, and vitamin B₁₂ into a single once-a-day dosage unit.

One of ordinary skill in the art would have been motivated to incorporate beta-blockers, such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors, such as pravastatin, folic acid, vitamin B₆, and vitamin B₁₂ into a single once-a-day dosage unit. All the agents herein: different beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, and vitamin B₆ are all known to reduce risk of cardiovascular

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diseases. Possessing the teachings of the cited prior art, combining two or more agents which are known to be useful to reduce risk of cardiovascular disease individually into a single sustained release, once-daily composition useful for the very same purpose is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069), absent evidence to the contrary. Furthermore, possessing the teaching of Oakley et al., one of ordinary skill in the art would incorporate vitamin B₁₂ into any folic acid containing composition including the instant composition since vitamin B₁₂ administration would prevent folic acid adverse effect such as vitamin B₁₂ deficiency.

Response to Arguments

Applicant's arguments filed June 26, 2003 averring the basis of combining the herein claimed actives relying on Rork have been considered, but are not found persuasive. The motivation to combine the herein claimed active compounds is provided by the cited prior art because all the agents herein: different beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, and vitamin B₆ are all known to reduce risk of cardiovascular diseases. Possessing the teachings of the cited prior art, combining two or more agents which are known to be useful to reduce risk of cardiovascular disease individually into a single sustained release, once-daily composition useful for the very same purpose is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069), absent evidence to the contrary. Furthermore, possessing the teaching of Oakley et al., one of ordinary skill in the art would incorporate vitamin B₁₂ into any folic acid containing

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composition including the instant composition since vitamin B₁₂ administration would prevent folic acid adverse effect such as vitamin B₁₂ deficiency.

Applicant's arguments filed June 26, 2003 averring the examiner inappropriately applying *In re Kerkhoven* have been considered, but are not found persuasive. Please note that although beta-blocker and statins have different kind of mechanism of action, they are useful for cardioprotection individually. Therefore, combining them together into a single composition useful for the very same thing is obvious.

Applicant's arguments filed June 26, 2003 averring the cited prior art's failure to teach the applicant's motivation for combining the herein claimed ingredients (beta-blockers, statins, and other active ingredients), i.e., to improve compliance in elderly patients, have been fully considered but they are not persuasive. Examiner notes that such motivation has never been recited in the claims. Arguments drawn to the unclaimed limitation is considered moot. Even if such limitation is recited in the claims, the intended use does not lend patentable weight in claims that are drawn to composition.

The declaration of Dr. Gurwitz filed June 26, 2003 in paragraphs 7-9 constructively argues long-felt need that the issue of non-compliance in elderly patients has not been resolved and the cited prior art have not addressed such issue. Therefore, the herein claimed invention would be unobvious to the cited prior art's teaching. Such arguments have been considered, but are not found persuasive. As discussed above, arguments drawn to the unclaimed limitation is considered moot. Even if such limitation is recited in the claims, the intended use does not lend patentable

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weight in claims that are drawn to composition. Furthermore, the evidences of improving compliance have not been demonstrated. It states that the claimed subject matter solved a problem that was long standing in the art. However, there is no showing that others of ordinary skill in the art were working on the problem and if so, for how long. In addition, there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. See MPEP § 716.04. In addition, the references provided by the applicants are all recently published (they are published in 2003). Non-obviousness of the invention has to be established at the time the invention was made. Therefore, these references are not pertinent to the showing of non-obviousness of the instant invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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San-ming Hui
Patent Examiner
Art Unit 1617


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